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HPV Curriculum

Genital Human Papillomavirus (HPV)

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HPV Curriculum

Learning Objectives

Upon completion of this content, the learner will be able to

1. Describe the epidemiology of genital HPV infection in the U.S.;
2. Describe the pathogenesis of genital HPV;
3. Discuss the clinical manifestations of genital HPV infection;
4. Identify methods used to diagnose genital warts and cervical cellular abnormalities;
5. Discuss CDC-recommended treatment regimens for genital warts;
6. Summarize appropriate prevention counseling messages for genital HPV infection;
7. Describe public health measures for the prevention of genital HPV infection.

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HPV Curriculum

Lessons

- I. Epidemiology of genital HPV infection in the U.S.
- II. Pathogenesis
- III. Clinical manifestations and sequelae
- IV. Diagnosis of genital warts and cervical cellular abnormalities
- V. Patient management
- VI. Patient counseling and education
- VII. Partner management and public health measures

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Lesson I: Epidemiology of Genital HPV Infection in the U.S.

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HPV Curriculum Epidemiology

Introduction

- Genital HPV is one of the most common STDs
- More than 40 HPV types can infect the genital tract

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HPV Curriculum Epidemiology

Introduction

- HPV types are divided into two groups based on their association with cancer.
 - Low-risk types (nononcogenic) associated with genital warts and mild Pap test abnormalities
 - High-risk types (oncogenic) associated with moderate to severe Pap test abnormalities, cervical dysplasia and cervical cancer, and other cancers
- Most genital HPV infections are transient, asymptomatic, and have no clinical consequences.

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HPV Curriculum Epidemiology

Incidence in the U.S.

- Estimated annual incidence of sexually-transmitted HPV infection is 14.1 million
- Estimated \$1.7 billion spent annually in direct medical costs to treat conditions associated with genital HPV infection

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HPV Curriculum Epidemiology

Prevalence in the U.S.

- 100% of sexually active men and women acquire genital HPV at some point in their lives.
- An estimated 79 million females aged 14–59 years are infected with HPV infection.

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HPV Curriculum Epidemiology

Incidence and Prevalence of HPV-associated Diseases

- Genital warts
 - Incidence may be as high as 100/100,000.
 - An estimated 1.4 million may be affected at any one time.
- Cervical cancer
 - Rates of cervical cancer have fallen by approximately 75% since the introduction of Pap screening programs.
 - Incidence is estimated at 8.1/100,000.

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Risk Factors for Men

- Risk increases with increasing number of recent and lifetime sex partners
- Being uncircumcised increases risk

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Lesson II: Pathogenesis

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HPV Curriculum Pathogenesis

Virology

- Double-stranded DNA virus that belongs to the *Papillomaviridae* family
- Genital types have specific affinity for genital skin and mucosa
- Infection identified by the detection of HPV DNA

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HPV Curriculum Clinical Manifestations

Clinical Manifestations and Sequelae

- In most cases, genital HPV infection is transient and has no clinical manifestations or sequelae.
- Clinical manifestations of genital HPV infection include
 - Genital warts,*
 - Cervical cellular abnormalities detected by Pap tests,*
 - Some anogenital squamous cell cancers,
 - Some oropharyngeal cancers, and
 - Recurrent respiratory papillomatosis.

*Two most common clinically significant manifestations of genital HPV infection

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HPV Curriculum Clinical Manifestations

Genital Warts-Appearance

- Condylomata acuminata
 - Cauliflower-like appearance
 - Skin-colored, pink, or hyperpigmented
 - May be keratotic on skin; generally nonkeratinized on mucosal surfaces
- Smooth papules
 - Usually dome-shaped and skin-colored
- Flat papules
 - Macular to slightly raised
 - Flesh-colored, with smooth surface
 - More commonly found on internal structures (i.e., cervix), but also occur on external genitalia
- Keratotic warts
 - Thick horny layer that can resemble common warts or seborrheic keratosis

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HPV Curriculum Clinical Manifestations

Genital Warts-Location

- Most commonly occur in areas of coital friction
- Perianal warts do not necessarily imply anal intercourse.
 - May be secondary to autoinoculation, sexual activity other than intercourse, or spread from nearby genital wart site
- Intra-anal warts are seen predominantly in patients who have had receptive anal intercourse.
- HPV types causing genital warts can occasionally cause lesions on oral, upper respiratory, upper GI, and ocular locations.
- Patients with visible warts are frequently simultaneously infected with multiple HPV types.

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HPV Curriculum Clinical Manifestations

Genital Warts-Symptoms

- Genital warts usually cause no symptoms. Symptoms that can occur include:
 - Vulvar warts-dyspareunia, pruritis, burning discomfort;
 - Penile warts-occasional itching;
 - Urethral meatal warts-hematuria or impairment of urinary stream;
 - Vaginal warts-discharge/bleeding, obstruction of birth canal (secondary to increased wart growth during pregnancy); and
 - Perianal and intra-anal warts-pain, bleeding on defecation, itching
- Most patients have fewer than ten genital warts, with total wart area of 0.5–1.0 cm².

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HPV Curriculum Clinical Manifestations

Genital Warts-Duration and Transmission

- May regress spontaneously, or persist with or without proliferation.
 - Frequency of spontaneous regression is unclear, but estimated at 10–30% within three months.
 - Persistence of infection occurs, but frequency and duration are unknown.
 - Recurrences after treatment are common.

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HPV Curriculum Clinical Manifestations

Genital Warts and High-Risk HPV

- High-risk HPV types occasionally can be found in visible warts and have been associated with squamous intrepithelial lesions (squamous cell carcinoma *in situ*, Bowenoid papulosis, Erythroplasia of Queyrat, or Bowen' s disease of the genitalia).
- The lesions can resemble genital warts.
- Unusual appearing genital warts should be biopsied.

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HPV Curriculum Clinical Manifestations

Genital Warts in Preadolescent Children

- May be due to sexual abuse although this condition is not diagnostic for sexual abuse. Their appearance should prompt an evaluation by a clinician.
- May also result from vertical transmission, transmission of nongenital HPV types to genital surface, and possibly fomite transmission, although fomite transmission has never been documented.

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HPV Curriculum Clinical Manifestations

Perianal Warts



Source: Seattle STD/HIV Prevention Training Center at the University of Washington/ UW HSCER Slide Bank

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HPV Curriculum Clinical Manifestations

Vulvar Warts



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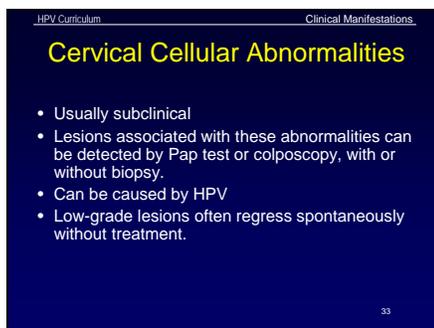
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HPV Curriculum Clinical Manifestations

Recurrent Respiratory Papillomatosis

- HPV infections in infants and children may present as warts in the throat, also known as juvenile onset recurrent respiratory papillomatosis (JORRP).
- Respiratory papillomatosis is a rare condition, usually associated with HPV types 6 and 11.

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Lesson IV: Diagnosis of Genital Warts and Cervical Cellular Abnormalities

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HPV Curriculum Diagnosis

Diagnosis of Genital Warts

- Diagnosis is usually made by visual inspection with bright light.
- Consider biopsy when
 - Diagnosis is uncertain;
 - Patient is immunocompromised;
 - Warts are pigmented, indurated, or fixed;
 - Lesions do not respond or worsen with standard treatment; or
 - There is persistent ulceration or bleeding.

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Diagnosis of Cervical Cellular Abnormalities

- Cytology (Pap test)
 - Useful screening test to detect cervical cell changes
 - Provides indirect evidence of HPV because it detects squamous epithelial cell changes that are almost always due to HPV

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Diagnosis of Cervical Cellular Abnormalities-continued

- HPV DNA tests
 - FDA-approved:
 - To triage women with ASC-US Pap test results, and
 - As an adjunct to Pap test screening for cervical cancer in women 30 years or older.
- HPV DNA tests should not be used
 - In men,
 - In adolescents <21 years,
 - To screen partners of women with Pap test abnormalities,
 - To determine who will receive HPV vaccine, or
 - STD screening for HPV.

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HPV Curriculum Diagnosis

Diagnosis of Cervical Cellular Abnormalities-continued

- Colposcopy
 - Indication guided by physical exam or Pap test findings with or without HPV DNA test findings
- Cervical biopsy
 - May be indicated if there is/are
 - Visible exophytic lesions on cervix
 - Pap test with HSIL, ASC-H, or other findings
- For more information on guidelines for managing women with cervical cytologic abnormalities, refer to 2006 Consensus Guidelines for Management of Women with Cervical Cytologic Abnormalities <http://www.asccp.org/consensus/cytological.shtml>

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Lesson V: Patient Management

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General Treatment of Genital Warts

- Primary goal is removal of warts.
- If left untreated, genital warts may regress spontaneously or persist with or without proliferation.
- In most patients, treatment can induce wart-free periods.
- Currently available therapies may reduce, but probably do not eliminate infectivity.
- Effect of current treatment on future transmission is unclear.

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General Treatment of Genital Warts-continued

- No evidence that presence of genital warts or their treatment is associated with development of cervical cancer.
- Some patients may choose to forgo treatment and await spontaneous resolution.
- Consider screening persons with newly diagnosed genital warts for other STDs (e.g., chlamydia, gonorrhea, HIV, syphilis).

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HPV Curriculum Management

Treatment Regimens

- Patient-applied and provider-administered therapies are available.
- Providers should be knowledgeable about and have available, at least one patient-applied and one provider-administered treatment.
- Choice of treatment should be guided by
 - Patient preference,
 - Available resources,
 - Experience of the healthcare provider,
 - Location of lesion(s), and
 - Pregnancy status.

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HPV Curriculum Management

Treatment Regimens-continued

- Factors influencing treatment selection include
 - Wart size,
 - Number of warts,
 - Anatomic site of wart,
 - Wart morphology,
 - Patient preference,
 - Cost of treatment,
 - Convenience, and
 - Adverse effects.

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HPV Curriculum Management

Treatment Response

- Affected by
 - Number, size, duration, and location of warts, and immune status
 - In general, warts located on moist surfaces and in intertriginous areas respond better to topical treatment than do warts on drier surfaces.
- Many patients require a course of therapy over several weeks or months rather than a single treatment.
 - Evaluate the risk-benefit ratio of treatment throughout the course of therapy to avoid over-treatment.
- There is no evidence that any specific treatment is superior to any of the others.
 - The use of locally developed and monitored treatment algorithms has been associated with improved clinical outcomes

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HPV Curriculum Management

CDC-Recommended Regimens For External Genital Warts (Patient-Applied)-continued

- **Using patient-applied treatments**
 - Provider should identify warts for treatment and teach patients how to apply substance.
 - Patient must be able to identify and reach warts to be treated.
 - Podofilox 0.5% solution or gel, an antimitotic drug that destroys warts, is relatively inexpensive, easy to use, and safe.
 - Most patients experience mild or moderate pain or local irritation after treatment with podofilox.
 - Imiquimod is a topically active immune enhancer that stimulates production of interferon and other cytokines.
 - Local inflammatory reactions are common with use of imiquimod and sinecatechins; these reactions include redness and irritation and are usually mild to moderate.
- **Follow-up is not required, but may be useful several weeks into therapy to determine appropriateness of medication use and response to treatment.**

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HPV Curriculum Management

CDC-Recommended Regimens For External Genital Warts (Provider-Administered)

- **Cryotherapy with liquid nitrogen or cryoprobe**
 - Repeat applications every 1–2 weeks, or
- **Podophyllin resin 10%–25%* in compound tincture of benzoin**
 - Apply a small amount to each wart and allow to air dry
 - To avoid toxicity
 - Application should be limited to < 0.5 mL of podophyllin or < 10 cm² of warts per session
 - No open lesions or wounds should exist in the area to which treatment is administered
 - Treatment may be repeated weekly if needed, or
- **Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%–90%**
 - Apply small amount only to warts and allow to dry
 - Treatment may be repeated weekly if needed, or
- **Surgical removal** - tangential scissor excision, tangential shave excision, curettage, or electrosurgery

*Safety not established in pregnancy

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Alternative Treatment Regimens

- **Alternative Treatment Regimens include treatment options that might be associated with more side effects and/or less data on efficacy including**
 - Intralesional interferon,
 - Carbon dioxide laser and surgery, and
 - Topical cidofovir.

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HPV Curriculum Management

CDC-Recommended Regimens for Exophytic Cervical Warts

- Biopsy needed, high-grade squamous intraepithelial lesions (SIL) must be excluded before treatment is initiated.
- Management should include biopsy and consultation with a specialist.

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CDC-Recommended Regimens for Vaginal Warts

Treat only if symptomatic, since most treatments also affect normal tissue and can cause scarring and pain.

- **Cryotherapy with liquid nitrogen**
 - Use of a cryoprobe in the vagina is not recommended because of risk for vaginal perforation and fistula formation.
- or
- **TCA or BCA 80%–90% applied to warts**
 - Apply small amount only to warts and allow to dry (white “frosting” develops).
 - Treatment may be repeated weekly if needed.

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CDC-Recommended Regimens for Urethral Meatal Warts

- **Cryotherapy with liquid nitrogen**
- or
- **Podophyllin 10%–25% in compound tincture of benzoin**
 - Treatment area must be dry before contact with normal mucosa.
 - Treatment may be repeated weekly, if needed.

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HPV Curriculum Management

CDC-Recommended Regimens for Anal Warts

- Cryotherapy with liquid nitrogen
or
- TCA or BCA 80%–90% applied to warts
 - Apply small amount only to warts and allow to dry (white “frosting” develops).
 - Treatment may be repeated weekly if needed.
- or
- Surgical removal

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HPV Curriculum Management

Management in Pregnancy

- Genital warts can proliferate and become more friable during pregnancy.
- Cytotoxic agents (podophyllin, podofilox, imiquimod) should not be used.
- Cryotherapy, TCA, BCA, and surgical removal may be used.
- HPV types 6 and 11 can cause recurrent respiratory papillomatosis in children. The route of transmission is not completely understood.
- Prevention value of cesarean delivery is unknown; thus, C-section should not be performed solely to prevent transmission to neonate.

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HPV Curriculum Management

Genital Warts in HIV-Infected Patients

- No data that treatment should be different
- Larger, more numerous warts
- Might not respond as well to therapy
- More frequent recurrence of lesions after treatment
- Squamous cell carcinomas arising in or resembling genital warts might occur more frequently among immunosuppressed persons, therefore, requiring biopsy for confirmation of diagnosis for suspicious cases, and referral to a specialist.

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HPV Curriculum Management

Treatment of Cervical Dysplasia

- For more information on managing women with cervical dysplasia, refer to the following sources:
 - 2006 Consensus Guidelines for the Management of Women with Cervical Cytologic Abnormalities <http://www.asccp.org/consensus/cytological.shtml>
 - CDC National Breast and Cervical Cancer Early Detection Program <http://www.cdc.gov/cancer/nbccedp/index.htm>

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HPV Curriculum

Lesson VI: Patient Counseling and Education

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HPV Curriculum Patient Counseling and Education

The Nature of HPV Infection

- Genital HPV infection is common in sexually active adults.
 - The majority of sexually active adults will have HPV infection at some point, although most will never know because infection will be asymptomatic and will clear on its own.
- Natural history of HPV infection is usually benign
 - Low-risk genital HPV types are associated with mild Pap test abnormalities and genital warts.
 - High-risk types are associated with mild to severe Pap test abnormalities and, rarely, cancers of the cervix, vulva, vagina, anus, penis, oropharynx.
 - Most women infected with HPV do not develop cervical cancer.
- Genital warts have a high recurrence rate after treatment.

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HPV Curriculum Prevention

Special Considerations

- Pregnant women should have a Pap test as part of routine prenatal care
- Anal Pap test screening in HIV-positive persons not routinely recommended

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HPV Curriculum Prevention

Reporting Requirements

- Genital HPV infection is not a reportable infection.
- Genital warts are reportable in some states.
- Some states have made cervical precancer reportable.
- Check with state or local health department for reporting requirements for HPV associated outcomes in your area.

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HPV Curriculum Prevention

HPV Vaccines

- Two types
 - Bivalent vaccine (HPV2) protects against HPV 16 and 18-associated cervical precancers.
 - Quadrivalent vaccine (HPV4) protects against HPV 6, 11, 16, and 18-associated genital warts, cervical precancers, vulvar and vaginal precancers, and anal precancers.
- Administration
 - Either vaccine is recommended for routine vaccination of females aged 11 or 12 years. HPV4 is recommended for routine vaccination of males aged 11 or 12 years. This vaccine can be given at 9 or 10 years of age.
 - Vaccination is also recommended for 13–26 year old females and 13–21 year old males who have not had any or all the doses at a younger age.
 - MSM should be vaccinated through age 26 years.
 - Immunocompromised persons (including those with HIV-infection) should be vaccinated through age 26 years.

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HPV Curriculum Prevention

HPV Vaccines (continued)

- Dosing
 - Three-dose series intramuscularly over a six-month period
- Women who have received HPV vaccine should continue routine cervical cancer screening.
 - Thirty percent of cervical cancers are caused by HPV types other than 16 and 18
- CDC has a website with additional vaccine information
<http://www.cdc.gov/vaccines/pubs/ACIP-list.htm#hpv>

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Case Study

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HPV Curriculum Case Study



History

- **Anne Drew:** 34-year-old woman who wants to get "checked out" because Jonathan, her sex partner, has small solid "bumps" on the skin on the shaft of his penis.
- Jonathan told her that he was diagnosed and treated for genital warts about a year ago, and his healthcare provider told him they could recur.
- No history of abnormal Pap smears and no history of STDs
- Last Pap smear performed 4 months ago
- Sexually active with men only since age 16; has had a total of 7 sex partners over her lifetime
- Currently sexually active with 1 partner for the last 8 months
- Uses oral contraceptives for birth control

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HPV Curriculum Case Study

Question

1. What should be included in Ms. Drew's evaluation?

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HPV Curriculum Case Study

Physical Examination

- Vital signs: blood pressure 96/74, pulse 78, respiration 13, temperature 37.1° C
- Cooperative, good historian
- Chest, heart, musculoskeletal, and abdominal exams within normal limits
- Pelvic exam is normal
- Visual inspection of the genitalia reveals multiple small (<0.5 cm), flesh-colored, papular lesions in the perineal area

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HPV Curriculum Case Study

Questions

2. What is the differential diagnosis for the papular genital lesions?
3. What is the **most likely** diagnosis based on history and physical examination?
4. Which laboratory tests should be ordered or performed?

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